



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/595,204

01/25/2008

Carsten Juergen Kirschning

RSW 86283 US

4608

65159

7590

03/30/2011

TechLaw LLP

10755 Scripps Poway Parkway, Suite 465

San Diego, CA 92131

EXAMINER

BUNNER, BRIDGET E

ART UNIT

PAPER NUMBER

1647

NOTIFICATION DATE

DELIVERY MODE

03/30/2011

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@techlawllp.com

david@techlawllp.com

Office Action Summary	Application No. 10/595,204	Applicant(s) KIRSCHNING ET AL.	
	Examiner Bridget E. Bunner	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 January 2011.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28,30 and 32-35 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 6 is/are allowed.
- 6) ☒ Claim(s) 1-5,7-28,30 and 32-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 March 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendments of 30 September 2010 and 25 January 2011 have been entered in full. Claims 1-8, 10, 12-18, 20, 21, 23, 28, 33 are amended. Claims 33-35 are added. Claims 29 and 31 are cancelled.

Claims 1-28, 30, and 33-35 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objections to the specification at page 3 of the previous Office Action (29 April 2010) are withdrawn in view of the amended abstract and specification (30 September 2010).
2. The objections to claims 6, 10, and 17 at pages 3-4 of the previous Office Action (10 April 2010) are withdrawn in view of the amended claims (30 September 2010).
3. The rejections of claims 3-6, 8-17, 19-22, 24-28, and 30 under 35 U.S.C. 112, second paragraph, as set forth at pages 4-5 of the previous Office Action (29 April 2010) are withdrawn in view of the amended claims (30 September 2010). Please see section on 35 U.S.C. 112, second paragraph below.
4. The rejection of claims 1-17, 22 under 35 U.S.C. § 112, first paragraph (scope of enablement) as set forth at pages 6-14 of the previous Office Action (29 April 2010) is withdrawn in view of the amended claims (30 September 2010 and 25 January 2011).
5. The rejection of claims 1-28 and 30 under 35 U.S.C. § 112, first paragraph (written description) as set forth at pages 16-19 of the previous Office Action (29 April 2010) is withdrawn in view of the amended claims (30 September 2010 and 25 January 2011).

New Claim Objections

6. Claims 1, 5, 23, 32, and 33 are objected to because of the following informalities:

6a. In claim 1, line 7, the number “64” in the phrase “residues 58-64” should be amended to recite “65”.

6b. In claim 1, line 12, the number “46” in the phrase “residues 46-56” should be amended to recite “47”.

6c. In claim 5, line 1, the term "regions" should be amended to recite "region".

6d. In claim 23, line 3, the term "regions" should be amended to recite "region".

6e. In claim 23, line 3, the phrase “the variable region of” is missing before "the light chain". Such language should be added for consistency since line 3 also recites “the variable region[s] of the heavy chain...”.

6f. In claim 23, line 3, for clarity, after the term “or both”, the following phrase should be inserted: “the variable region of the heavy chain of said antibody and the variable region of the light chain of said antibody”.

6g. In claim 23, since there are several lengthy members of the Markush group, it is suggested that each be separated by a semi-colon, rather than a comma. For instance, “...the antibody of claim 1 or a fragment thereof; a nucleic acid encoding the variable region of the heavy chain of said antibody, the variable region of the light chain of said antibody, or both the variable region of the heavy chain of said antibody and the variable region of the light chain of said antibody; or, a vector comprising said nucleic acid...”.

6h. 6g. In claim 33, line 3, the number “64” in the phrase “residues 58-64” should be amended to recite “65”.

Art Unit: 1647

6i. In claim 33, line 9, the number “46” in the phrase “residues 46-56” should be amended to recite “47”.

Appropriate correction is required.

Maintained and New Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-5, 7-28, 30, 32, 33, and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 7, 8, 18, 23, and 33 are indefinite because the elements recited in the claim do not constitute proper Markush groups. The claims are indefinite in the alternative use of “and/or” because it is not clear what controls which of these limitations. See MPEP § 2173.05(h). The basis for this rejection is set forth for claims 3-28 and 30 at page 4 of the previous Office Action (29 April 2010) and it was indicated which specific claims recited the “and/or” language (i.e., claims 3-7, 18, 20, 23).

At page 11 of the Response of 30 September 2010, Applicant indicates that claims 4, 5, 6, 7, 18, 20, 21, and 23 have been amended to revise the “and/or” terminology. Although many of the claims have been amended to remove the “and/or” language, claims 7, 18, 23 (and new claim 33) still contain this phrase.

9. Claims 1-5, 8-28, 30, 32-34 are rejected as being indefinite because the claims refer to particular amino acid sequences with SEQ ID NOs recited in parentheses (for instance, claim 1,

Art Unit: 1647

line 7, “the amino acid sequence Gly-Phe-Thr-Phe-Thr-Thr-Tyr-Gly (residues 58-64 of SEQ ID NO: 2)”. However, SEQ ID NOs: 1 and 2 (which are both referred to in the claims) are directed to nucleic acid sequences, and not amino acid sequences. The specific nucleic acid residues referred to in the parentheses does not match the amino acid sequence recited in the claims.

Hence, it is not clear if the claims are attempting to encompass an antibody encoded by nucleic acid sequences or if the claims are attempting to encompass an antibody comprising amino acid sequences, with reference to incorrect SEQ ID NOs. It is noted that the heavy and light chain amino acid sequences are SEQ ID NOs: 6 and 7, respectively.

10. Claims 7-8 are rejected as being indefinite because it is not clear what nucleic acids are encompassed by the phrase "one or more nucleic acids selected from Nos. 172-201, 244-292, 385-417 of SEQ ID NO: 1, or of nucleic acids No. 130-174, 2209-240 and/or 337-363 of SEQ ID NO: 2". For instance, does the claim encompass a nucleic acid molecule comprising nucleic acids 172-201, 244-292, and 385-417 of SEQ ID NO: 1? A nucleic acid comprising nucleic acids 130-174, 220-240, and/or 337-363 of SEQ ID NO: 2? Does the claim encompass one, two, three, four, five, and/or six of these specific nucleic acid ranges? Or, does the claim encompass a nucleic acid fragment that has one or more nucleic acids within the ranges recited in the claim?

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claim 35 is rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The claim reads on a product of nature in that the claimed antibody

Art Unit: 1647

is not “isolated”. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of “isolated” or “purified” as taught by page 24, 3rd full paragraph and page 29 of the specification. See MPEP 2105.

Maintained Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 18-21, 23-28, and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: (i) a pharmaceutical composition comprising said cross-reactive antibody of claim 1 and (ii) a method of preventing or treating TLR2-induced septic shock in a mammal comprising administering to said mammal the isolated cross-reactive antibody, **does not reasonably provide enablement for** pharmaceutical compositions comprising nucleic acids or a vector; a method of preventing or treating a TLR2 mediated process; and a method of treatment by administering a nucleic acid or vector. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The basis for this rejection is set forth at pages 14-16 of the previous Office Action of 29 April 2010.

Claim 18 is directed to a pharmaceutical composition comprising the antibody or fragment thereof of claim 1, a nucleic acid encoding the variable regions of the heavy and/or

Art Unit: 1647

light chains of said antibody or a vector comprising said nucleic acid and a pharmaceutically acceptable carrier. Claim 23 recites a method of preventing and/or treating a TLR2-mediated process in a mammal comprising administering the antibody of claim 1, a nucleic acid encoding the variable regions of the heavy chain of said antibody, the light chain of said antibody, or both, or a vector comprising said nucleic acid or a composition comprising any thereof and a pharmaceutically acceptable carrier to said mammal in an effective amount to prevent and/or treat said TLR2-mediated process. Claim 30 recites that the TLR2-mediated process of claim 23 is selected from rheumatoid arthritis, vascular arthritis, and inflammatory bowel disease.

It is noted that at the bottom of page 14 of the Response of 30 September 2010, Applicant states that without acceding to the correctness of these objections and solely to progress the prosecution of this application, references to variants and parts have been deleted from the amended claim set.

The Examiner acknowledges that Applicant has amended the claims to address the variant and host cell issues raised by the Examiner at points (i) and (ii) of the scope of enablement rejection at pages 6-14 of the previous Office Action of 29 April 2010. However, Applicant has not addressed the issue set forth at point (iii) at pages 14-16 of the previous Office Action. For Applicant's convenience, the issue is herein reiterated below.

At page 16, last paragraph, the specification teaches that the antibody, nucleic acid, vector or composition of the invention are used in the prevention and/or treatment of inflammatory processes or any other process induced by bacterial infection, trauma, or chronic inflammation. The specification also adds that they can be used for the prevention and/or treatment of bacteraemia or sepsis, rheumatoid arthritis, vascular arthritis, or inflammatory

bowel disease. As mentioned previously, the specification only discloses that in mice given T2.5 either prior (1h) or up to 2 h after or *B. subtilis* microbial challenge, all or *B. subtilis* challenged mice survived (page 26, bottom of 1st full paragraph; Figure 6b). The specification adds that treatment of T2.5 3 h after potentially lethal injection saved 75% of the mice challenged (page 26, bottom of 1st full paragraph; Figure 6b). However, the specification does not teach any methods or working examples that indicate that TLR2 cross-reactive antibodies, nucleic acids, or vectors prevent or treat all TLR2-mediated processes (including rheumatoid arthritis, vascular arthritis, and inflammatory bowel disease), other than TLR2-driven septic shock. Relevant literature teaches that the role of TLR2 in many diseases or conditions is not certain or predictable. For example, McCormack et al. disclose that elevated levels of TLR2 have been found in macrophages isolated from rheumatoid arthritis synovium (*Arthritis Res Therapy* 11(5): 243, 2009;; page 244, column 2, 2nd paragraph). However, McCormack et al. also disclose that IL1rn-/-TLR2-/- animals develop severe arthritis, suggesting an anti-inflammatory role for TLR2 in that model (page 244, column 2, 3rd full paragraph). McCormack et al. state that the anti-inflammatory nature of TLR2 in the IL1-receptor antagonist knockout model is in contrast to results obtained in a streptococcal cell wall induced model of arthritis, where mice deficient for TLR2 have reduced severity of arthritis (page 244, column 2, 3rd full paragraph). Cario, E. also teaches that deficient TLR2 signaling may imbalance commensal-dependent intestinal epithelial barrier defense, facilitating mucosal injury and leading to increased susceptibility to colitis (*Mucosal Immunol* 1(Suppl 1): S62-S66, 2008; abstract). Specifically, Cario discloses that loss of TLR2 leads to exacerbation of intestinal inflammation in DSS colitis with high morbidity and mortality (page S64, bottom of column 1 through column 2). Cario indicates that treatment with

Art Unit: 1647

a synthetic TLR2 ligand significantly suppresses mucosal inflammation in vivo (page S64, column 2, last paragraph). Hence, in view of the lack of guidance in the instant specification and the contradictory state of the art, there is no clear nexus or mechanism between TLR2 and TLR2-mediated processes, other than TLR2-induced septic shock. A large quantity of experimentation would be required of the skilled artisan to identify the nexus between TLR2 and all TLR2-mediated processes and administer cross-reactive antibodies, nucleic acids, or vectors for prevention or treatment. Such experimentation is considered undue. As was found in Ex parte Hitzeman, 9 USPQ2d 1821 (BPAI 1987), a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. See also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991). The present invention is unpredictable and complex wherein one skilled in the art may not necessarily prevent or treat all possible TLR2-mediated processes in a mammal by administering cross-reactive TLR2 antibodies, nucleic acids, or vectors. It is also noted that the specification does not teach any methods or working examples that indicate a heavy or light chain nucleic acid of SEQ ID NO: 1 or 2 (or a vector comprising such) is introduced and expressed in a cell for therapeutic purposes.

As discussed in section (ii) at pages 12-14 of the previous Office Action, the specification also discloses that the present invention "is directed to a gene therapy approach for use in the treatment of chronic diseases. The approach basically follows the already known protocols for gene therapy and comprises in particular the step of cloning a sequence comprising the variable

Art Unit: 1647

domains of the antibody of the invention as specified above into an expression vector and introducing said expression vector into a host, for example a human patient in order to cause an overexpression of said antibody/antibody fragment in said patient” (page 17, 1st paragraph). However, the specification does not teach any methods or working examples that indicate a heavy or light chain nucleic acid of SEQ ID NO: 1 or 2 (or a vector comprising such) is introduced and expressed in a cell for therapeutic purposes. The disclosure in the specification is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. For example, the specification does not teach what type of vector would introduce the nucleic acids into the cell or in what quantity and duration. Relevant literature teaches that since 1990, about 3500 patients have been treated via gene therapy and although some evidence of gene transfer has been seen, it has generally been inadequate for a meaningful clinical response (Phillips, A., J Pharm Pharmacology 53: 1169-1174, 2001; abstract). Additionally, the major challenge to gene therapy is to deliver DNA to the target tissues and to transport it to the cell nucleus to enable the required protein to be expressed (Phillips, A.; pg 1170, ¶ 1). Phillips also states that the problem with gene therapy is two-fold: 1) a system must be designed to deliver DNA to a specific target and to prevent degradation within the body, and 2) an expression system must be built into the DNA construct to allow the target cell to express the protein at therapeutic levels for the desired length of time (pg 1170, ¶ 1). Therefore, undue experimentation would be required of the skilled artisan to introduce and express a nucleic acid into the cell of an organism. Additionally, gene therapy is unpredictable and complex wherein one skilled in the art may not necessarily be able to introduce and express a nucleic acid

Art Unit: 1647

molecule of SEQ ID NO: 1 or 2 in the cell of an organism or be able to produce a protein in that cell.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation to treat all possible TLR2-mediated processes and to introduce and express a heavy chain or light chain nucleic acid in a cell of an organism for therapy; the lack of direction/guidance presented in the specification regarding the same; the absence of working examples directed to the same; the complex nature of the invention that establishes the unpredictability of transferring genes into an organism's cells; and the breadth of the claims, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

New Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 7 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Queen et al. (U.S. Patent 5,530,101).

Queen et al. teach an isolated nucleic acid which comprises one or more nucleic acids numbered 130-174, 220-240, and 337-363 of SEQ ID NO: 2 of the instant application. For example, Queen et al. teaches nucleic acids 130-137, 139-149, and 337-345 of SEQ ID NO: 2 of the instant application (see nucleic acids 130-137, 139-149, and 337-345 of SEQ ID NO: 66 of

Art Unit: 1647

Queen et al.; see also the sequence alignment attached to the instant Office Action as Appendix

A). Queen et al. teach that DNA sequences will further include an expression control DNA sequence operably linked to the humanized immunoglobulin coding sequences (column 16, lines 43-59; column 17, lines 61-64).

Conclusion

Claim 6 is allowable.

Claims 1-5, 7-28, 30, 32-35 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Art Unit: 1647

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571)272-0881. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB
Art Unit 1647
15 March 2011

/Bridget E Bunner/
Primary Examiner, Art Unit 1647

Art Unit: 1647

Appendix A

Qy= SEQ ID NO: 2 of the instant application

Db=sequence of Queen et al.

```
US-07-634-278-66
; Sequence 66, Application US/07634278
; Patent No. 5530101
; GENERAL INFORMATION:
;   APPLICANT: QUEEN, Cary L.
;   APPLICANT: CO, Man Sung
;   APPLICANT: SCHNEIDER, William P.
;   APPLICANT: LANDOLFI, Nicholas F.
;   APPLICANT: COELINGH, Kathleen L.
;   APPLICANT: SELICK, Harold E.
;   TITLE OF INVENTION: IMPROVED HUMANIZED IMMUNOGLOBLINS
;   NUMBER OF SEQUENCES: 113
;   CORRESPONDENCE ADDRESS:
;     ADDRESSEE: Townsend and Townsend Khourie and Crew
;     STREET: 379 Lytton Avenue
;     CITY: Palo Alto
;     STATE: California
;     COUNTRY: US
;     ZIP: 94301
;   COMPUTER READABLE FORM:
;     MEDIUM TYPE: Floppy disk
;     COMPUTER: IBM PC compatible
;     OPERATING SYSTEM: PC-DOS/MS-DOS
;     SOFTWARE: PatentIn Release #1.0, Version #1.25
;   CURRENT APPLICATION DATA:
;     APPLICATION NUMBER: US/07/634,278
;     FILING DATE: 19-DEC-1990
;     CLASSIFICATION: 424
;   PRIOR APPLICATION DATA:
;     APPLICATION NUMBER: US 07/590,274
;     FILING DATE: 28-SEP-1990
;   PRIOR APPLICATION DATA:
;     APPLICATION NUMBER: US 07/310,252
;     FILING DATE: 13-FEB-1989
;   PRIOR APPLICATION DATA:
;     APPLICATION NUMBER: US 07/290,975
;     FILING DATE: 28-DEC-1988
;   ATTORNEY/AGENT INFORMATION:
;     NAME: Smith, William M
;     REGISTRATION NUMBER: 30,223
;     REFERENCE/DOCKET NUMBER: 11823-002600
;   TELECOMMUNICATION INFORMATION:
;     TELEPHONE: (415) 326-2400
;     TELEFAX: (415) 326-2422
;   INFORMATION FOR SEQ ID NO: 66:
;     SEQUENCE CHARACTERISTICS:
;       LENGTH: 393 base pairs
;       TYPE: nucleic acid
;       STRANDEDNESS: single
;       TOPOLOGY: linear
;     MOLECULE TYPE: cDNA
;     FEATURE:
;       NAME/KEY: CDS
;       LOCATION: 1..393
```


Art Unit: 1647

US-07-634-278-66

```
Query Match          77.2%;  Score 341.8;  DB 2;  Length 393;
Best Local Similarity 91.9%;
Matches 361;  Conservative 0;  Mismatches 32;  Indels 0;  Gaps 0;

Qy      1  ATGGAGTCAGACACACTCCTGCTATGGGTGCTGCTGCTCTGGGTTCCAGGCTCCACTGGT  60
      |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||
Db      1  ATGGAGAAAGACACACTCCTGCTATGGGTCTGCTTCTCTGGGTTCCAGGTTCCACAGGT  60

Qy      61  GACATTGTGCTCACCCAATCTCCAGCTTCTTTGGCTGTGTCTCTAGGGCAGAGAGCCACC 120
      |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||
Db      61  GACATTGTGCTGACCCAATCTCCAGCTTCTTTGGCTGTGTCTCTAGGGCAGAGGGCCACC 120

Qy     121  ATCTCCTGCAGAGCCAGTGAAAGTGTTGAATATTATGGCACAAAGTTTAAATGCAGTGGTAC 180
      |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||
Db     121  ATCTCCTGCAGAGCCAGCGAAAGTGTTGATAATTATGGCATTAGTTTTATGAACTGGTTC 180

Qy     181  CAACAGAAACCAGGACAGCCACCCAAACTCCTCATCTTTGGTGCATCCAACGTAGAATCT 240
      |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||
Db     181  CAACAGAAACCAGGACAGCCACCCAAACTCCTCATCTATGCTGCATCCAACCAAGGATCC 240

Qy     241  GGGGTCCCTGTCAGGTTTCAGTGGCAGTGGGTCTGGGACAGACTTCAGCCTCAACATCCAT 300
      |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||
Db     241  GGGGTCCCTGCCAGGTTTAGTGGCAGTGGGTCTGGGACAGACTTCAGCCTCAACATCCAT 300

Qy     301  CCTGTGGAGGAGGATGATATTGTAATGTATTTCTGTCAGCAAAGTAGGAAACTTCCGTGG 360
      |||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||
Db     301  CCTATGGAGGAGGATGATACTGCAATGTATTTCTGTCAGCAAAGTAAGGAGGTTCCGTGG 360

Qy     361  ACGTTCGGTGGAGGCACCAAGCTGGAATCAAA 393
      |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||
Db     361  ACGTTCGGTGGAGGCACCAAGCTGGAATCAAA 393
```